Title:

The role of interleukin-24 in the pathomechanism of IBD-associated tissue remodeling

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Abstract:

Introduction: Intestinal fibrosis is a serious complication of inflammatory bowel diseases (IBD). Interleukin(IL)-24 is a member of IL-20 cytokine subfamily, which regulatory effect is suspected in connection with inflammation, apoptosis or tissue remodeling in other organs. Increased level of IL-24 was described in the colon of patients with active IBD, however its biological role is still poorly understood.

Methods: Colonic presence of IL-24 and its receptor IL-20RB was investigated in the dextran-sodium sulfate (DSS) induced mice model of IBD (n=8; C57BL/6J). Impact of IL-24 on colonic extracellular matrix (ECM) production was investigated in the DSS treated wild type and IL-20RB knockout (KO) mice. Effect of intracolonic injection of IL-24 was also investigated. The role of IL-24 treatment on the expression of fibrosis related genes was investigated in colonic epithelial (HT-29) and fibroblast (CCD-18Co) cells.

Results: Expression of IL-24 increased in colonic tissue of DSS-treated mice compared to controls. Lack of IL-24 receptor resulted in reduced ECM deposition in IL-20RB KO mice compared to wild type group. Local administration of IL-24 increased the expression of the fibrosis associated genes in the colon. IL-24 treatment increased the expression of TGF-ß1 and PDGF-B in HT-29, and that of COL1, COL3, FN1, MMP2, -9, TIMP1, -2 in CCD-18Co cells.

Discussion: IL-24 may promote tissue remodeling shifted toward an excessive deposition of ECM components directly by acting on fibroblast and indirectly via induction of pro-fibrotic factors on epithelial cells. Our data suggest that inhibition of IL-24 may have a significant anti-fibrotic effect.

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